ABSTRACT

The present invention relates to a method of detecting variant nucleic acid whose nucleotide sequence differs from one another at a single (or more) position(s). The method uses a set of chimeric oligonucleotides containing DNA monomers and monomers of a novel class of DNA analogues, locked nucleic acid (LNA). LNA oligomers obey the Watson-Crick base-pairing rules and form duplexes that are significantly more stable than similar duplexes formed by DNA. The "allele-specific" LNA-containing oligonucleotides wherein the LNA nucleotide(s) are found at the 3' position can be extended by means of enzymes only where the nucleotide(s), which is/are terminal in direction of extension, is/are complementary to the corresponding nucleotides of the nucleic acid (of the one allele) to be detected. Thus discrimination between alleles without subsequent differential hybridization with labelled oligonucleotides is possible. The invention further relates to reagents for performing the methods as well as applications of the method.